

REMARKS

The present application is a continuation-in-part of PCT/JP01/10234 filed November 22, 2001. Claims 1-19 were presented at the time of filing. In response to a Restriction Requirement dated November 1, 2005, Applicant elected the claims of Group I (claims 1-3 and 15-19); claim 15 was cancelled and rewritten as new claim 20. Claims 1-14 and 16-20 were, therefore, pending in the application with claims 4-14, 18 and 19 withdrawn from consideration as being directed to an unelected invention. Claim 2 is cancelled above. Claims 1, 3-14 and 16-20 remain pending in the application with claims 4-14, 18 and 19 withdrawn from consideration.

Specification

The Office Action asserts that the title of the invention is not descriptive. Accordingly, the title is amended above in accordance with the Examiner's suggestion.

Claim Objections

Claims 1 and 16 are objected to in that the recitation of "SMG-1" is viewed as an improper abbreviation. In Applicant's view, gene and protein names are not abbreviations, but rather designations that are made in accordance with nomenclature conventions well known to those of skill in the art. Notwithstanding the above, the claims are amended herein to include the functional characteristic of the protein from which the name derives.

The designation "SMG-1," is well known to those skilled in the art and refers to a protein first identified as a suppressor of morphogenetic effect on genitalia-1 in *Caenorhabditis elegans* (see Morita, T. et al., "Distant N-terminal and C-terminal domains are required for intrinsic kinase activity of SMG-1, a critical component of nonsense-mediated mRNA decay", J. Biol. Chem., a copy of which is enclosed for the Examiner's convenience).

Claim 1 is objected to as using a confusing format. Claim 1 is amended above to more clearly identify the isolated polypeptides that Applicant considers the invention. Support for the amendment to claim 1 can be found on page 12, line 31 to page 13, line 5 of the present specification.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 16 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 16 and 20 are amended above to recite a mutant SMG-1 polypeptide that lacks SMG-1 activity. Support for the amendment can be found in the specification at page 5, lines 16-20.

A “mutant,” as that term is meant in the art, refers to a molecule or organism that differs from the wild-type. Sometimes the mutation is silent; in other cases, it results in a different phenotype. In the present case, the mutant SMG-1 polypeptide has lost the SMG-1 activity associated with the wild-type (non-mutant) polypeptide.

In view of the above, withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

Rejection under 35 U.S.C. §101

Claims 1-3 and 16-17 are rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter, specifically, the claimed polypeptides allegedly read on a product of nature. Accordingly, the claims are amended above to indicate the hand of the inventor, that is, the term “isolated” has been inserted in the claims to clarify that the claimed peptide is not a naturally occurring polypeptide.

In view of the above amendment, withdrawal of the rejection under 35 U.S.C. §101 is respectfully requested.

Rejection Under 35 U.S.C. § 112, first paragraph

***New Matter Rejection***

Claims 16 and 20 are rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement, specifically, the office action states that the claims contain subject matter that was not described in the specification in a manner to reasonably convey to one skilled in the art that the inventor(s) had possession of the claimed invention at the time the application was filed.

Claims 16 and 20 are amended herein to clearly indicate that the present invention, as claimed herein, is intended to encompass a mutant SMG-1 polypeptide that is SMG-1 activity deficient, that is, does not have SMG-1 activity. Support for the amendment is found in the description of agents for suppressing nonsense mediated mRNA decay at page 5, lines 16-20.

***Written Description***

Claims 1-2, 16-17, and 20 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claim 2 is canceled above. The rejection with respect to homologous polypeptides is therefore, moot.

Claim 1 is amended above to recite a polypeptide that comprises a specific base sequence (amino acids 129-3657 of SEQ ID NO: 2) and limited variants thereof, specifically, polypeptides in which 1-5 amino acid residues of amino acids 129-3657 of SEQ ID NO: 2 are deleted or substituted, or in which 1-5 amino acids are inserted.

The adequacy of a patent disclosure is judged from the perspective of one of ordinary skill in the art (*Falkner, Holzer, and Dorner*, 05-1324, Fed. Cir. 2006). The Federal Circuit has stated that a claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for the person of skill in the art and the skilled artisan is presumed to bring with her a knowledge of what has come before. Thus, in the present case, given the base structure of the claimed polypeptide, one of skill can readily imagine all the members of the genus.

#### ***Enablement***

Claims 1-2, 16-17, and 20 are rejected under 35 U.S.C. 112, first paragraph because, according to the Office Action, the specification does not reasonably provide enablement for all variants of SEQ ID NO:2 including SEQ ID NO:2 with a single mutation with a mutation from Asp to Ala at position 2331. The Office Action acknowledges that the specification is enabling for the polypeptide of SEQ ID NO:2.

An application satisfies the enablement requirement if one skilled in the art, after reading the disclosure, could practice the invention claimed without undue experimentation *In re Wands*, 858 F.2d 731. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation “must not be unduly extensive.” *Chiron Corporation v. Genentech, Inc.*, 363 F.3d 1247.

Like the inquiry with respect of the written description requirement, the adequacy of the disclosure with respect to enablement is judged from the perspective of the skilled artisan. In the present case, the skilled artisan would have several years experience in recombinant techniques such as site-direct mutagenesis for generating polypeptides with point mutations an enzyme assay experienc, therefore, having the needed technical skill to practice some experimentation as described in the scientific literature relating to and providing background for the present

invention.

Preliminarily, a patent disclosure need not enable information within the knowledge of an ordinary artisan. In the instant case, all of the methodology required for making the variants identified by Applicants is well known to those of skill in the biochemical art. Independent claim 1 is amended above and is focused on a limited number of variants and provides guidance for testing whether the variant SNG-1 polypeptides may be screened for their ability to suppress nonsense-mediated mRNA decay. Applicants respectfully submit that the claims, as amended herein, are adequately enabled.

Clearly, no additional guidance is necessary and no undue experimentation is required for one of skill to practice the claimed method.

In view of the above arguments, withdrawal of the rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 1-2 and 16-17 are rejected under 35 U.S.C. § 102(a) as being anticipated by Denning et al. (*J. Biol. Chem.* 276: 22709-22714, 2001). According to the Office Action, Denning et al. teaches isolation of an SMG-1 polypeptide, which has the ability to phosphorylate Upf1p or kinase-deficient SMG-1 mutants. Additionally, the Office Action states that the polypeptide is 99.7% similar to Applicant's claimed polypeptide, thereby anticipating the claims of the present application.

Claim 1, as amended above, is directed to an isolated polypeptide comprising amino acids 129-3657 of SEQ ID NO:2 or an isolated polypeptide in which 1-5 amino acids of 129-3657 of SEQ ID NO: 2 are deleted, substituted, and/or inserted. The polypeptide of the invention,

therefore has a base sequence consisting of 3528 amino acids.

Denning et al. teaches a human orthologue of *C. elegans* SMG-1 that is a protein of 3031 amino acids rather than one of 3528 amino acids. As shown in the alignment document submitted herewith, the protein of Denning et al. (amino acids 1-3031) corresponds to amino acids 627-3657 of the present invention. That is, the SMG-1 protein of Denning et al. lacks 626 amino acids of the amino terminus of Applicant's claimed SMG-1 protein, including amino acids 129 to 626 of SEQ ID NO: 2. It should be noted that there is a significant difference between the sequence of the present application and the Denning protein, specifically, the Denning protein lacks the long N-terminal region of amino acids 1-626 in SEQ ID NO: 2 of the present application. Therefore, while the protein taught by Denning et al. is highly homologous (99.7%) to a portion of the claimed human SMG-1 protein, Denning et al. does not teach an isolated polypeptide comprising amino acids 129-3657 of SEQ ID NO: 2, nor does Denning et al. teach a polypeptide that is 90% homologous to that polypeptide.

In support of his position, Applicant submits herewith a comparison between the protein of SEQ ID NO: 2 of the present application ("hsmglaa" in Attachment A) and the protein disclosed in the Denning et al. reference ("JBCsmlg" in Attachment A). The "hsmglaa" protein has 3657 amino acids and the "JBCsmlg"/ Denning protein has 3031 amino acids. The region of amino acids 627-3657 in the "hsmglaa" protein is identical to that of amino acids 1-3031 in the Denning et al. protein except for the following four amino acids:

hsmglaa:	Ala (682)	Arg (739)	Phe (1189)	Arg (2005)
JBCsmlg	Ser (56)	Lys (113)	Cys (563)	Lys (1379)

The homology of 99.87% [= (3031-4/3031 x 100(%))] extends only to this overlapping region and cannot be construed as applying to the protein overall.

Thus, the protein taught by Denning et al. cannot anticipate the SMG-1 protein claimed by Applicant and withdrawal of the rejection under 35 U.S.C. 102 in view of Denning et al. is respectfully requested.

Claims 1-3 and 16-17 are also rejected under 35 U.S.C. § 102(a) as being anticipated by Ohnishi et al. (23<sup>rd</sup> Annual Meeting of the Molecular Biology Society of Japan, Program and Abstracts, December 14, 2000).

Submitted herewith is a Declaration of Shigeo Ohno to the effect that he is the sole inventor of the present invention, and that the other authors of the publication cited were merely working under his direction. Accordingly, the rejection of the present claims under 35 U.S.C. § 102(a) as being anticipated by the knowledge or use “by others” is overcome and withdrawal of the rejection is respectfully requested.

Claims 1-3 and 16-17 are also rejected under 35 U.S.C. 102(a) as anticipated by Yamashita et al. (*Genes Develop* 15: 2215, 2001). The priority date of the present application is May 24, 2001, and submitted herewith is a verified English translation of the certified copy of the priority document, Japanese patent application No. 2001-156088. The Yamashita et al. reference was not accepted by the journal until July 6, 2001, and therefore, would not have been available to the public prior to that date. Thus, Yamashita et al. is unavailable as prior art in rejecting the present invention.

Lastly, claims 1-2 and 16-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Loughney et al. (U.S. Patent 6,344,549). According to Appendix C, the ATR-2 protein disclosed in the Loughney et al. reference is composed of 2930 amino acids, and the region of amino acids 728-2657 in the hSMG-1 protein of the present invention is identical to that of amino acids 1-2390 in the “ATR-2” protein, except for the following two amino acids:

hSMG-1      Arg ( 739)      Phe (1189)  
ATR-2      Lys ( 12)      Cys ( 462)

The homology of this overlapping region is 99.93% [= (2930-2)/2930 X 100(%)].

Like the protein taught by Denning et al., the ATR-2 protein taught by Loughney et al. lacks a significant portion of SEQ ID NO:2, specifically, the long terminal region of amino acids 1-727 in SEQ ID NO: 2 of the present application. Thus, while certain regions of the ATR-2 protein are highly homologous to SEQ ID NO: 2, Loughney et al., does not teach an isolated polypeptide comprising amino acids 129-3657 of SEQ ID NO: 2). Thus, the present invention is not anticipated by Loughney et al.

In view of the above arguments, withdrawal of the rejection under 35 U.S.C. §102 in view of Loughney et al. is respectfully requested.

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Serial No. 10/720,460  
Filed: November 24, 2003  
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It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

  
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Dated: March 20, 2007

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